

A DNA construct comprising:

a first DNA segment encoding a precursor polypeptide comprising a pro-sequence of a mammalian t-PA; and

a second DNA segment operably linked to the first DNA sequence, the second DNA sequence encoding a heterologous glycoprotein.

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- . The DNA construct of claim 1 wherein the heterologous glycoprotein is an immunoadhesin.
- 3. The DNA construct of claim 2 wherein the immunoadhesin is a TNF receptor immunoadhesin.
- The DNA construct of claim 3 wherein the TNF receptor immunoadhesin is TNFR1-IgG1.

operably linked to a pre-sequence other than a mammalian t-PA pre-sequence.

6. The DNA construct of claim 5 wherein the heterologous glycoprotein is and immunoadhesin.

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The DNA construct of claim 6 wherein the immunoadhesin is a TNF receptor immunoadhesin.

8. The DNA construct of claim 7 wherein the TNF receptor immunoadhesin is TNFR1-IgG1.

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- 9. The DNA construct of claim 5 wherein the mammalian t-PA pro-sequence is operably linked a presequence associated with the native heterologous polypeptide.
- 10. The DNA construct of claim 9 wherein the heterologous glycoprotein is a TNF receptor immunoadhesin and the pre-sequence is a pre-sequence of a mammalian TNF receptor.
- 11. The DNA construct of claim 10 wherein the mammalian t-PA pro-sequence is SEQ ID NO: 7.
- 12. The DNA construct of claim 11 wherein the pre-sequence is SEQ ID NO: 8.
- 13. The DNA construct of claim 12 wherein the TNF receptor immunoadhesin is TNFR1-IgG1.

July 14.

A DNA construct comprising:

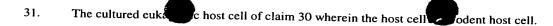
a first DNA segment encoding a precursor peptide; and

a second DNA segment operably linked to the first DNA sequence, the second DNA sequence encoding a heterologous glycosylation site variant glycoprotein.

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- 15. The DNA construct laim 14 further comprising one or more add and DNA segments operably linked to the first and second DNA segments.
- 16. The DNA construct of claim 14 wherein the precursor peptide comprises the pro-sequence of a mammalian t-PA.
- 17. The DNA construct of claim 16 wherein the pro-sequence is a human t-PA pro-sequence.
- 18. The DNA construct of claim 17 wherein the pro-sequence is SEQ ID NO: 5.
- 19. The DNA construct of claim 16 further comprising a pre-sequence of a mammalia t-PA.
- 20. The DNA construct of claim 19 wherein the pre-sequence is a human t-PA pre-sequence.
- 21. The DNA construct of claim 20 wherein the pre-sequence is SEQ ID NO: 3.
- 22. The DNA construct of claim 21 wherein the precursor peptide is SEQ ID NO 1.
- 23. The DNA construct of claim 14 wherein the heterologous glycosylation site variant is a glycosylation site addition variant.
- 24. The DNA construct of claim 14 wherein the heterologous glycosylation site variant is a glycosylation site deletion variant.
- 25. The DNA construct of claim 24 wherein the heterologous glycosylation site variant is an immunoadhesin.
- 26. The DNA construct of claim 25 wherein the immunoadhesin is TNFR-IgG.
- 27. The DNA construct of claim 26 wherein the TNFR-IgG is TNFR1-IgG1.
- 28. The DNA construct of claim 27 wherein the TNFR1-IgG1 has an N-linked glycosylation site selected from the group consisting of amino acid positions 14, 105, 111 and 248 deleted.
- 29. The DNA construct of claim 28 wherein the TNFR1-IgG1 has the N-linked site at 14 deleted.
- A cultured eukaryotic host cell comprising a DNA construct comprising:

  a first DNA segment encoding a precursor peptide corresponding to a mammalian tissue plasminogen activator secretory peptide; and
- a second DNA segment operably linked to the first DNA sequence, the second DNA sequence encoding a heterologous glycosylation site variant.



32. The cultured cukaryotic host cell of claim 31 which is a CHO cell.

- 33. A method of producing a polypertide which has been altered to delete one or more native N-linked glycosylation sites comprising the steps of
  - (a) culturing a eukaryotic host cell comprising a DNA construct comprising:
- a first DNA segment encoding a precursor peptide corresponding to a mammalian tissue plasminogen activator signal-pro peptide; and
- a second DNA segment operably linked to the first DNA sequence, the second DNA sequence encoding a heterologous glycosylation site deletion variant polypeptide;

wherein the eukaryotic host cell express the first and second DNA segments and the polypeptide is secreted from the cell; and

(b) recovering the polypeptide so produced.

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